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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,105	MALIGA ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *3,6,7 and 18-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5 and 8-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-28 are pending.

2. This application contains claims 3, 6-7 and 18-28 drawn to inventions nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-2, 4-5 and 8-17 are examined to the extent they read on plasmids comprising SEQ ID NO:14.

5. The drawings remain objected to because Figure 24 is black boxes. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

6. The objection to claims 4-5, 8-10, 12-14 and 16-17 because of informalities is withdrawn in light of Applicant's amendments to the claims.

7. The objection to claim 5 is being a substantial duplicate of claim 2 is withdrawn in light of Applicant's amendment to claim 5.

Claim Rejections - 35 USC § 112

8. Claims 15-17 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated

for the reasons of record as set forth in the Office action mailed 3 July 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the plasmids are sufficiently described so that they can be made without undue experimentation and pointed to pages in the specification (response pg 11-13).

This is not found persuasive. pMSK45 is said a "derivative" of pMSK35 (pg 81, lines 1-3), but how it was made from pMSK35 and how it differs from pMSK35 is not specified. pMSK48 is made from pMSK45 by inserting in a fragment made using primers that encode a particular peptide sequence (pg 80, line 26, to pg 81, line 1); but as many different nucleic acids can encode a particular peptide, the sequence in pMSK48 is not taught. Thus, the specification does not teach the making of pMSK45 and pMSK48.

Applicant urges that the sequence of pMSK35 is shown in Figures 33A-B (response pg 12.

This is acknowledged, and the rejection, insofar as it applied to pMSK35, is withdrawn. The rejection is maintained for plasmids pMSK45 and pMSK48.

9. Claims 1-2 and 8-14 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003, as applied to claims 1-2, 5 and 8-14. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the fact pattern of the instant case is very different from Eli Lilly because in that case the claimed subject matter was never described; in the instant case a

multiplicity of downstream box sequences are described, meeting the standards of Eli Lilly for a "reasonable" number (response pg 14-15).

This is not found persuasive. In Eli Lilly, a rat insulin gene was described, but this did not describe the genus of vertebrate insulin genes. In the instant case a few downstream boxes are described, but because it appears, based on the guidance in Figure 2, that a downstream box is merely any sequence that can basepair with the 26 base long anti-downstream box region by as few as 5 exact matches and 3 weak G-U matches, the genus of downstream boxes appears to be almost any sequence. The specification does not describe a representative number of all DNAs.

Applicant urges that pg 3 and 23-24 and Figs 1 and 3 describe exemplary downstream box elements, methods of determining them, and 5' regulatory regions comprising downstream box elements (response pg 15).

This is not found persuasive because the description of the structural features of a few exemplary downstream box elements do not comprise a description of the structural features of a representative number of all downstream box elements, given that downstream box elements appear to be almost any DNA sequence.

10. Claims 1-2 and 8-14 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA constructs comprising some plastid downstream box sequences, does not reasonably provide enablement for DNA constructs comprising all plastid downstream box sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003, as applied to claims 1-2, 5 and 8-14.

This is not found persuasive because whether a construct is encompassed by the claim would depend on the intended use for the construct - in other words, if the construct comprises a coding region that encoded a protein from tobacco, if one wished to use that construct to transform rice, the construct would be encompassed in the claim, but it would not be encompassed if one intended to use that same construct to transform tobacco. This makes the claim indefinite because it is not clear if a particular construct is encompassed by the claim.

Applicant urges that breadth is not indefiniteness (response pg 19).

This is not found persuasive because the claim is not being rejected for its breadth, but for the use of "heterologous" which, as the example above shows, is a relative term.

Claim 1 lacks antecedent basis for the limitation "said chimeric regulatory region" in line 7. Applicant makes no arguments with respect to this rejection. It is noted that the amendment to insert "chimeric" before "5' regulatory region" in lines 3-4 does not provide antecedent basis for said chimeric regulatory region" in line 7.

Claim 10 is indefinite in its recitation of "said fusion protein encoded by a first and second coding region" in lines 2-3.

Applicant urges that components of the coding region and the nucleic acid encoding are clear from the claim as originally recited, although Applicant has amended it (response pg 20).

This is not found persuasive because while the first and second coding regions are operably linked to the 5' regulatory region, they do not appear to be operably linked to each other. Does this that the fusion protein is encoded by more than one coding region?

Claim 14 is indefinite in its recitation of "said construct comprising a sequence selected from the group of SEQ ID NOS:21-25 and 27." SEQ ID NOs:21-25 are FLARE coding

Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that considerable experimentation is permissible as long as it is not undue; one of skill in the art could use conventional genetic engineering techniques to develop constructs containing putative downstream domains and test them for enhanced transnational efficiency using the techniques described in the specification (response pg 16-17).

This is not found persuasive. Based on the guidance in Figure 2 it appears that a downstream box is merely any sequence that can basepair with the 26 base long anti-downstream box region by as few as 5 exact matches and 3 weak G-U matches. This would encompass almost any sequence. The specification does not which of these sequences would actually function as downstream box sequences. The specification must teach how to make function downstream boxes within the full scope of the claims, not how to find them.

11. Claims 1-2, 4-5, and 8-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.
The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

It is unclear in claim 1, lines 2 and 6-7, what the protein is heterologous to - the plant? the promoter? the leader? the downstream box element?

Applicant urges that the protein is heterologous to the plant, citing the Encyclopedia of Molecular Biology (response pg 18-19).

sequences, not entire plasmids, while SEQ ID NO:27 is the entire sequence for the plasmid pMSK49.

Applicant urges that members of a Markush group do not have to be equal (response pg 21).

This is not found persuasive. Because SEQ ID NO:27 is the plasmid pMSK49, the claim is drawn to a DNA construct comprising a plasmid. How is that possible?

Claim Rejections - 35 USC § 102

12. Claims 1-2 remain rejected under 35 U.S.C. 102(b) as being anticipated by Svab et al (1993, Proc. Natl. Acad. Sci. USA 90:913-917) taken with the evidence of Maliga et al (US Patent 5,877,402, filed January, 1994). The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003, as applied to claims 1-2 and 5. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the identification of potential downstream boxes in the rejection does not meet the limitations of the instant claims because operably linked refers to two different regions spliced together; in Svab et al the downstream box element is within the coding region of the heterologous protein (response pg 22-23).

This is not found persuasive. The specification, on pg 9, lines 11-14 states "Operably-linked: refers to two different regions or two separate genes spliced together in a construct such that both regions will function to promote gene expression and/or protein translation." The aadA gene would comprise two regions spliced together; one region comprises the downstream box, which would be part of the 5' regulatory region, and the rest of the coding sequence is the other region.

Applicant urges that the instantly claimed invention requires that the chimeric regulatory region enhance translational efficiency, while Svab et al is silent as to whether the downstream box elements present in aadA increase translational efficiency (response pg 23).

This is not found persuasive. The increase in translational efficiency would be inherent to the presence of the downstream boxes, because the downstream boxes fall within the guidance provided in the instant specification in Figure 2, where it appears that a downstream box is merely any sequence that can basepair with the 26 base long anti-downstream box region by as few as 5 exact matches and 3 weak G-U matches.

The MPEP in section 2112 states: "'[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted].' The burden of proof is similar to that required with respect to product-by-process claims. In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977))."

13. Claims 1-2 and 9 remain rejected under 35 U.S.C. 102(e) as being anticipated by Maliga et al (US Patent 5,877,402, filed January, 1994) taken with the evidence of Jefferson (1993, GenBank Accession No. A00196). The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003, as applied to claims 1-2, 5 and 9. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the identification of potential downstream boxes in the rejection does not meet the limitations of the instant claims because the patent fails to teach or describe a

5' chimeric regulatory region comprising a downstream box operably linked to and increasing expression of a heterologous protein (response pg 23-24).

This is not found persuasive for the reasons outline above.

Applicant urges that downstream box in the patent is within the coding region of the heterologous protein and therefore is not part of the 5' chimeric regulatory region (response pg 23).

This is not found persuasive because the aadA, uidA and kan genes would comprise two regions spliced together; one region comprises the downstream box, which would be part of the 5' regulatory region, and the rest of the coding sequence is the other region.

Applicant urges that the patent is not by another because it is Applicant's own work (response pg 23).

This is not found persuasive because no declaration under 1.132 was made.

14. Claims 1-2 and 9 remain rejected under 35 U.S.C. 102(e) as being anticipated by McBride et al (US Patent 6,271,444, filed July 1998) taken with the evidence of Barry et al (1997, US Patent 5,627,061). The rejection is repeated for the reasons of record as set forth in the Office action mailed 3 July 2003, as applied to claims 1-2, 5 and 9. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the identification of potential downstream boxes in the rejection does not meet the limitations of the instant claims because the patent fails to teach or describe a 5' chimeric regulatory region comprising a downstream box operably linked to and increasing expression of a heterologous protein, while the downstream box in the patent is within the coding region of the heterologous fusion protein and therefore is not part of the 5' chimeric regulatory region (response pg 24-25).

This is not found persuasive for the reasons above.

15. Claims 4-5 are free of the prior art, given the failure of the prior art to teach or suggest a 5' regulatory region comprising SEQ ID NO:14. Claims 8 and 10-14 are free of the prior art, given the failure of the prior art to teach DNA construct comprising a 5' regulatory region operably linked to a synthetic bar DNA of SEQ ID NO:19 or 20 or a DNA encoding a fusion protein between a selectable marker and GFP, wherein the 5' regulatory region comprises a promoter, a leader sequence, and a downstream box. Claims 15-17 are free of the prior art, given the failure of the prior art to teach or suggest plastid transformation vectors pHK38(A), pMSK48, pMSK49 or pMSK35.

16. Claims 4-5 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 27, 2004